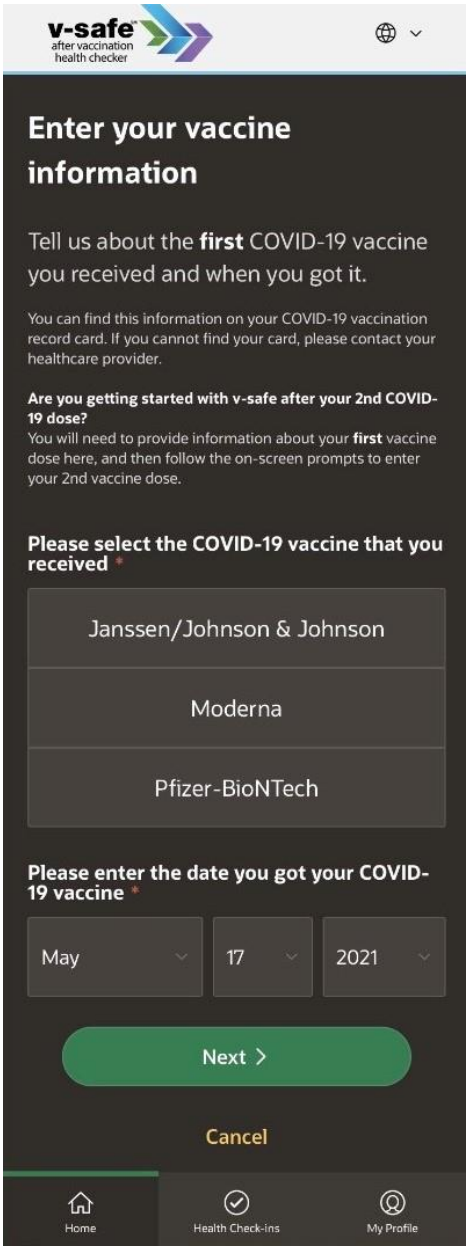
Supplemental Material

A. Survey visuals and interval timing

The full v-safe protocol is publicly available (https://www.cdc.gov/vaccinesafety/pdf/V-safe-Protocol-508.pdf). Figure A1 shows example visuals of v-safe as displayed on participant smartphones. Figure A2 demonstrates the survey interval timing by dose.

Figure A1. Example visuals of the v-safe survey



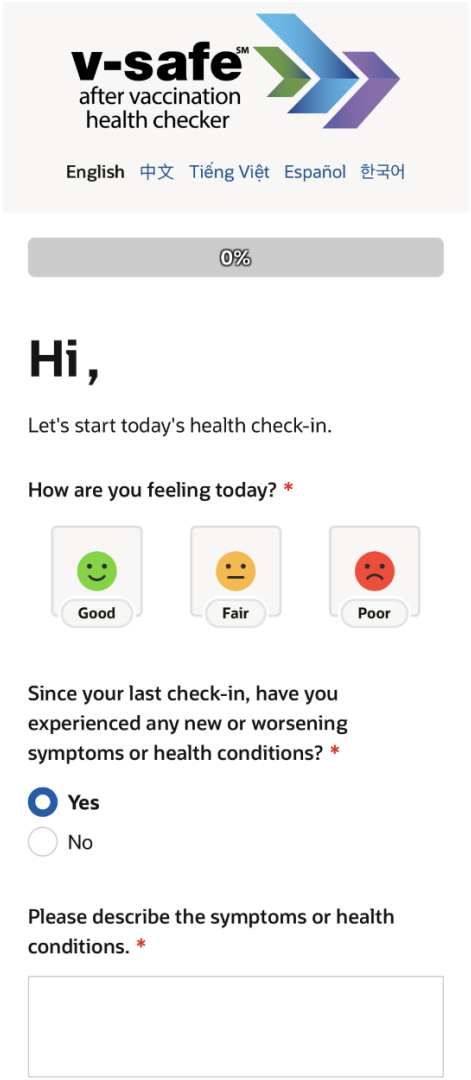
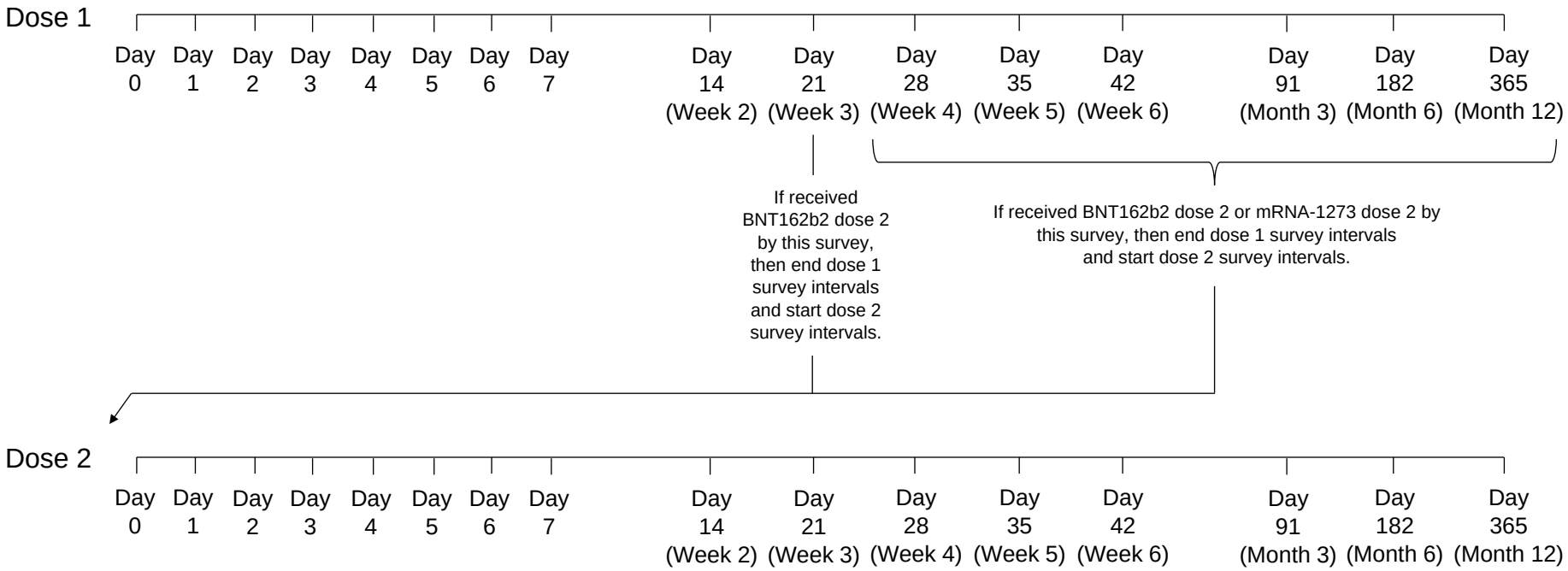


Figure A2. V-safe survey interval timing by dose



B. Text search methods

Phase 1

A list of key terms was developed to capture common reactions that align with those asked in v-safe daily surveys (Table B1). Additional reactions related specifically to injection site rash and "COVID arm" were included to capture common manifestations of delayed injection site reactions reported in the literature. Special characters and spaces were removed from text strings prior to the case-insensitive search. We evaluated terms that could be common roots for other words unrelated to the reaction of interest, as these could lead to false positives. For these key terms, the unmodified text string with spaces was used and a word boundary rule was applied (i.e., a non-word character or beginning or ending of the string was required before and after the key term); these terms are denoted with an asterisk (*) in the table. If a given search term was found in the text response of a participant, the participant was classified as having that corresponding outcome; if none of the key terms associated with a given outcome were found or the participant reported having no symptoms on the day 14 survey, the participant was classified as not having the corresponding outcome. Only English terms were used in this analysis; participants that provided a text response in a language other than English were not included.

Table B1. Key search terms for each reaction construct

Reaction constructs	Key Terms
Injection site	injectionsite|vaccinesite|vaccinationsite|shotsite|siteofinjection|siteofvaccine|siteofvaccination|siteofshot|siteoftheinjection|siteofthevaccine|siteofthevaccination|siteoftheshot|siteofmyinjection|siteofmyvaccine|siteofmyvaccination|siteofmyshot|atsite|atthesite|aroundsite|aroundthesite|aroundinjection|aroundvaccine|aroundvaccination|aroundshot|aroundtheinjection|aroundthevaccine|aroundthevaccination|aroundtheshot|aroundmyinjection|aroundmyvaccine|aroundmyvaccination|aroundmyshot|injectionarea|vaccinearea|vaccinationarea|shotarea|areaofinjection|areaofvaccine|areaofvaccination|areaofshot|areaoftheinjection|areaofthevaccine|areaofthevaccination|areaoftheshot|areaofmyinjection|areaofmyvaccine|areaofmyvaccination|areaofmyshot|whereinjection|wherevaccine|wherevaccination|whereshot|wheretheinjection|wherethevaccine|wherethevaccination|wheretheshot|wheremyinjection|wheremyvaccine|wheremyvaccination|wheremyshot|whereIhadinjection|whereIhadvaccine|whereIhadvaccination|whereIhadshot|whereIhadtheinjection|whereIhadthevaccine|whereIhadthevaccination|whereIhadtheshot|whereIhadmyinjection|whereIhadmyvaccine|whereIhadmyvaccination|whereIhadmyshot|whereIgotinjection|whereIgotvaccine|whereIgotvaccination|whereIgotshot|whereIgottheinjection|whereIgotthevaccine|whereIgotthevaccination|whereIgottheshot|whereIgotmyinjection|whereIgotmyvaccine|whereIgotmyvaccination|whereIgotmyshot|whereIreceivedinjection|whereIreceivedvaccine|whereIreceivedvaccination|whereIreceivedshot|whereIreceivedtheinjection|whereIreceivedthevaccine|whereIreceivedthevaccination|whereIreceivedtheshot|whereIreceivedmyinjection|whereIreceivedmyvaccine|whereIreceivedmyvaccination|whereIreceivedmyshot|localreaction|sitereaction|arm*
Pain	pain*|pains|painful|hurt|sore*|soreness
Redness	red*|redness*|reddened
Swelling	swelling|swollen|inflammation|inflamed|inflammed|inflammatory
Itching	itch*|itching*|itchy|itchiness|itched*|itches*
Rash	rash|skinreaction
COVID arm	covidarm
Injection site pain	Injection site AND Pain
Injection site redness	Injection site AND Redness
Injection site swelling	Injection site AND Swelling
Injection site itching	Injection site AND Itching
Injection site rash	Injection site AND Rash
Any injection site reaction	Injection site pain OR Injection site redness OR Injection site swelling OR Injection site itching OR Injection site rash OR COVID arm
Fatigue	fatigue|tired*|tiredness|exhaustion|exhausted|malaise|lethargy|lethargic
Headache	headache|migraine
Myalgia	myalgia|muscleache|musclesache|bodyache|backache|achiness|stiffness|achy*|aching*
Chills	chills|chill*

Fever	fever*|fevers|feverish|temperature|temp*
Joint Pain	joint|arthritis|arthralgia
Nausea	nausea|nauseous
Vomiting	vomit|throwingup|threwup
Diarrhea	diarrhea|loosestool
Abdominal Pain	abdominalpain|stomachpain|abdominalache|stomachache|abdominalcramping|stomachcramping|abdominalcramps|stomachcramps
Rash outside of injection site	rash|skinreaction|hives|shingles AND NO Injection site

Phase 2

To assess the validity of the selected key terms, we performed manual review of a random sample of 500 text responses (250 from dose 1, day 14 survey and 250 from dose 2, day 14 survey). The manual review assigned the appropriate values for each outcome of interest for each text response. Outcomes based on the text search algorithm were then compared to the outcomes based on manual review; measures of validity were calculated.

Table B2. Measures of validity for key terms classification compared to manual review of text responses

	Sensitivity	**Specificity**	**PPV**	**NPV**	**Accuracy**
Any injection site reaction[1]	81.6%	97.3%	86.6%	96.2%	98.0%
Injection site pain	85.0%	97.9%	63.0%	99.4%	99.0%
Injection site redness	77.8%	100.0%	100.0%	98.3%	99.4%
Injection site swelling	52.2%	98.7%	66.7%	97.7%	99.6%
Injection site itching	78.9%	99.8%	96.8%	98.3%	99.4%
Injection site rash	83.9%	100.0%	100.0%	98.9%	99.0%
COVID arm	100.0%	100.0%	100.0%	100.0%	99.6%
Any systemic reaction[2]	94.5%	94.3%	93.7%	95.0%	96.2%
Fatigue	100.0%	99.1%	94.5%	100.0%	99.2%
Headache	98.8%	99.0%	95.4%	99.8%	99.8%
Myalgia	63.2%	98.5%	77.4%	97.0%	96.2%
Chills	100.0%	99.4%	84.2%	100.0%	99.4%
Fever	100.0%	96.9%	55.9%	100.0%	99.0%
Joint Pain	85.2%	99.8%	95.8%	99.2%	99.4%
Nausea	100.0%	99.4%	88.0%	100.0%	99.6%
Vomiting	100.0%	100.0%	100.0%	100.0%	99.6%
Diarrhea	79.3%	100.0%	100.0%	98.7%	99.8%
Abdominal Pain	77.8%	100.0%	100.0%	99.2%	100.0%
Rash outside of injection site	89.5%	99.8%	94.4%	99.6%	99.0%

Abbreviations: PPV, positive predictive value; NPV, negative predictive value

[1]Any of the listed injection site reactions.

[2]Any of the listed systemic reactions.

For variables that did not meet an 80% threshold for sensitivity, specificity, positive predictive value, or negative predictive value, we manually reviewed text responses for participants with discordant classifications (i.e., false positives and false negatives) to identify potential refinements to the key terms. Table B3 shows the changes that were made.

Table B3. Refinement of terms

Reaction constructs	Key Terms
Injection site	ADDED: localized|injectionsight|vaccinesight|vaccinationsight|shotsight|sightofinjection|sightofvaccine| sightofvaccination|sightofshot|sightoftheinjection|sightofthevaccine|sightofthevaccination| sightoftheshot|sightofmyinjection|sightofmyvaccine|sightofmyvaccination|sightofmyshot| atsight|atthesight|aroundsight|aroundthesight EDITED: arm* IF NOT underrightarm|underleftarm|underarm|undermyarm|armpit
Pain	ADDED: tenderness EDITED: pain* IF NOT no pain* sore* IF NOT sorethroat
Redness	ADDED: reddish|pink|erythema|erythematous
Swelling	ADDED: raised|welt
Myalgia	ADDED: musclesoreness|musclessoreness|soremuscle|bodysoreness|sorebody|musclepain|musclespain| backpain|neckpain|muscleandjointpain|musclesandjointpain EDITED: bodyache IF NOT nobodyache
Fever	EDITED: fever* IF NOT no fever* AND IF NOT feverblister fevers IF NOT nofevers temperature IF NOT notemperature temp* IF NOT no temp*
Diarrhea	ADDED: loosebowel|dairrhea
Abdominal pain	ADDED: paininabdomen|abdominaldiscomfort

After this refinement process, we performed manual review of a second random sample of 500 text responses (250 from dose 1 day 14 survey and 250 from dose 2 day 14 survey) and assigned the appropriate values for each outcome of interest for each text response. Outcomes based on the refined text search algorithm were then compared to the outcomes based on manual review for this second sample; measures of validity were calculated as shown in Table B4.

Table B4. Post-refinement measures of validity for key terms classification compared to manual review of a second random sample

	Sensitivity	Specificity	PPV	NPV	Accuracy
Any injection site reaction[1]	93.0%	99.3%	96.9%	98.3%	98.0%
Injection site pain	90.9%	99.4%	87.0%	99.6%	99.0%
Injection site redness	94.2%	100.0%	100.0%	99.3%	99.4%
Injection site swelling	96.9%	99.8%	96.9%	99.8%	99.6%
Injection site itching	96.8%	99.6%	93.8%	99.8%	99.4%
Injection site rash	97.3%	99.1%	90.0%	99.8%	99.0%
COVID arm	83.3%	99.8%	83.3%	99.8%	99.6%
Any systemic reaction[2]	94.5%	97.7%	97.4%	95.2%	96.2%
Fatigue	98.5%	99.3%	95.6%	99.8%	99.2%
Headache	100.0%	99.8%	98.8%	100.0%	99.8%
Myalgia	74.1%	99.1%	91.5%	96.7%	96.2%
Chills	93.3%	99.6%	87.5%	99.8%	99.4%
Fever	100.0%	99.0%	82.1%	100.0%	99.0%
Joint Pain	88.2%	100.0%	100.0%	99.4%	99.4%
Nausea	100.0%	99.6%	92.3%	100.0%	99.6%
Vomiting	85.7%	99.8%	85.7%	99.8%	99.6%
Diarrhea	96.2%	100.0%	100.0%	99.8%	99.8%
Abdominal Pain	100.0%	100.0%	100.0%	100.0%	100.0%
Rash outside of injection site	90.5%	99.4%	86.4%	99.6%	99.0%

Abbreviations: PPV, positive predictive value; NPV, negative predictive value

[1]Any of the listed injection site reactions.

[2]Any of the listed systemic reactions.

Validity of measures increased substantially after refinement of the key terms. The sensitivity of myalgia was suboptimal but upon manual review of discordant records, it was determined that further refinement of terms could result in a reduction of positive predictive value. Therefore, no further refinement was conducted and the current key terms were used in main analyses.

C. Subanalysis of day 7 surveys completed between days 8 to 13 after vaccination

Days 8 to 13 following vaccination

The day 7 survey can only be completed once, but a participant can respond to this survey between days 7 to 13 following a given vaccine dose. Participants are asked about reactions they experienced "today" on the specific day they complete the survey. Participants that completed the day 7 survey on day 7 post-vaccination were included in analysis for days 0 to 7 for comparability to clinical trials. Persons completing the day 7 survey on day 7 since vaccination would not have had an opportunity to complete a survey on day 8 to 13; their second-week post-vaccination experiences would be reflected on the day 14 survey. Text message reminders were sent on day 9 to participants who had not yet completed their day 7 survey. A subanalysis was performed for persons who completed the one-time day 7 survey on any day from 8 to 13 post-vaccination. The number and percentage of participants that reported a given solicited reaction on the survey were assessed by vaccine dose and product.

A total of 862,367 participants had reported receiving dose 1 of an mRNA COVID-19 vaccine by March 14, 2021 and completed the day 7 survey between days 8 to 13 after dose 1. Of these, 48.0% received the BNT162b2 (Pfizer-BioNTech) vaccine and 52.0% the mRNA-1273 (Moderna) vaccine. A total of 440,768 participants had reported receiving dose 2 of an mRNA COVID-19 vaccine by March 14, 2021 and completed the day 7 survey between days 8 to 13 after dose 2 (50.6% BNT162b2 and 49.4% mRNA-1273). By vaccine product, the sex distribution was similar and the age distribution was slightly younger for BNT162b2; this was consistent for both dose 1 and dose 2 (Table D1). Of these participants, 15.0% reported an injection site reaction and 13.8% reported a systemic reaction on days 8-13 after dose 1. A slightly lower percentage was observed for injection site reactions during this period after dose 2 (10.6%) (Table D2). Differences by vaccine product were most pronounced for injection site reactions after dose 1 (20.7% mRNA-1273 vs. 8.9% BNT162b2). Small differences were found for injection site reactions after dose 2 (11.7% mRNA-1273 vs. 9.6% BNT162b2) and for systemic reactions after dose 1 (15.1% mRNA-1273 vs. 12.5% BNT162b2) or after dose 2 (15.0% mRNA-1273 vs. 13.9% BNT162b2).

Overall, injection site reactions reported on days 8 to 13 were most common after dose 1 of the mRNA-1273 vaccine, at about twice that of dose 1 BNT162b2 recipients. Systemic reactions were generally similar across doses and vaccine products. One key limitation of this subanalysis is that assessment of reactions on days 8 to 13 consisted of participants who did not complete their day 7 survey on time and may have responded only because they experienced an adverse reaction or they were reminded.

Table C1. Characteristics of v-safe participants completing the day 7 survey between days 8 to 13[1] following vaccination—CDC v-safe surveillance system, December 14, 2021 through March 28, 2021

	Both vaccines				BNT162b2				mRNA-1273			
	Dose 1 (N=862,367)		Dose 2 (N=440,768)		Dose 1 (N=413,638)		Dose 2 (N=223,156)		Dose 1 (N=448,729)		Dose 2 (N=217,612)	
	n	%	n	%	n	%	n	%	n	%	n	%
Manufacturer												
BNT162b2	413,638	48.0	223,156	50.6	–	–	–	–	–	–	–	–
mRNA-1273	448,729	52.0	217,612	49.4	–	–	–	–	–	–	–	–
Age (years)[2]												
<45	319,180	37.0	164,481	37.3	164,315	39.7	88,358	39.6	154,865	34.5	76,123	35.0
45-54	152,985	17.7	78,639	17.8	76,452	18.5	41,266	18.5	76,533	17.1	37,373	17.2
55-64	152,361	17.7	72,083	16.4	73,883	17.9	37,071	16.6	78,478	17.5	35,012	16.1
≥65	237,840	27.6	125,564	28.5	98,988	23.9	56,461	25.3	138,852	30.9	69,103	31.8
Not reported	1	–	1	–	0	–	0	–	1	–	1	–
Sex[2]												
Female	570,234	67.0	292,600	67.4	271,477	66.5	149,723	68.1	298,757	67.4	142,877	66.6
Male	280,371	32.9	141,336	32.5	136,483	33.4	70,010	31.4	143,888	32.5	71,326	33.3
Other	590	0.1	315	0.1	238	0.1	143	0.1	352	0.1	172	0.1
Not reported	11,172	–	6,517	–	5,440	–	3,280	–	5,732	–	3,237	–

Abbreviations: COVID-19 = coronavirus disease 2019

[1] The day 7 survey can be completed once between days 7 to 13 following a given vaccine dose; therefore persons completing the day 7 survey on day 7 since vaccination were not included in this table; their second-week post-vaccination experiences would be reflected on the day 14 survey.

[2] 'Not reported' categories are presented for clarity but not included in calculation of column percentages for the respective variable.

Table C2. Number and percentage of v-safe participants reporting local and systemic reactions to mRNA COVID-19 vaccines on the day 7 survey completed between days 8 to 13[1] following vaccination—CDC v-safe surveillance system, December 14, 2021 through March 28, 2021

	Both vaccines				BNT162b2				mRNA-1273			
	Dose 1 (N=862,367)		Dose 2 (N=440,768)		Dose 1 (N=413,638)		Dose 2 (N=223,156)		Dose 1 (N=448,729)		Dose 2 (N=217,612)	
	n	%	n	%	n	%	n	%	n	%	n	%
Any injection site reaction[2]	129,546	15.0	46,926	10.6	36,806	8.9	21,485	9.6	92,740	20.7	25,441	11.7
Injection site pain	90,219	10.5	37,469	8.5	32,370	7.8	18,680	8.4	57,849	12.9	18,789	8.6
Injection site redness	45,327	5.3	7,679	1.7	3,535	0.9	2,189	1.0	41,792	9.3	5,490	2.5
Injection site swelling	39,877	4.6	8,824	2.0	4,559	1.1	3,042	1.4	35,318	7.9	5,782	2.7
Injection site itching	44,427	5.2	10,332	2.3	4,252	1.0	2,907	1.3	40,175	9.0	7,425	3.4
Any systemic reaction[3]	119,329	13.8	63,688	14.4	51,729	12.5	31,043	13.9	67,600	15.1	32,645	15.0
Fatigue	57,458	6.7	32,976	7.5	25,090	6.1	15,794	7.1	32,368	7.2	17,182	7.9
Headache	48,469	5.6	27,312	6.2	21,537	5.2	13,093	5.9	26,932	6.0	14,219	6.5
Myalgia	31,942	3.7	18,504	4.2	13,467	3.3	8,699	3.9	18,475	4.1	9,805	4.5
Chills	11,439	1.3	8,741	2.0	4,717	1.1	3,569	1.6	6,722	1.5	5,172	2.4
Fever	10,154	1.2	4,818	1.1	4,413	1.1	2,219	1.0	5,741	1.3	2,599	1.2
Joint Pain	19,075	2.2	12,337	2.8	8,113	2.0	5,664	2.5	10,962	2.4	6,673	3.1
Nausea	12,243	1.4	6,689	1.5	5,380	1.3	3,137	1.4	6,863	1.5	3,552	1.6
Vomiting	1,607	0.2	968	0.2	742	0.2	433	0.2	865	0.2	535	0.2
Diarrhea	9,822	1.1	4,546	1.0	4,454	1.1	2,225	1.0	5,368	1.2	2,321	1.1
Abdominal Pain	6,446	0.7	3,324	0.8	2,924	0.7	1,585	0.7	3,522	0.8	1,739	0.8
Rash outside of injection site	7,306	0.8	2,652	0.6	2,089	0.5	1,220	0.5	5,217	1.2	1,432	0.7

Abbreviations: COVID-19 = coronavirus disease 2019

[1]The day 7 survey can be completed once between days 7 to 13 following a given vaccine dose; therefore persons completing the day 7 survey on day 7 since vaccination were not included in this table; their second-week post-vaccination experiences would be reflected on the day 14 survey.

[2]Any of the listed injection site reactions.

[3]Any of the listed systemic reactions.